Remarks / Arguments

Claims 82, 84-96, and 98-120 are pending in this application.

Claims 82, 85-88, 90, 93, 96, 98, 100, and 102, are withdrawn from consideration as being drawn to non-elected inventions. However, Applicants retain the right to present these claims in this Application, or a continuation, continuation-in-part, or divisional application of this Application.

Applicants respectfully request reconsideration of claims 84, 89, 91-92, 94-95, 99, 101 and 103-120 based on the following remarks.

I. Rejections Under 35 U.S.C. § 103(a)

Claims 89, 91-92, 94-95, 97, 99, 101, 103, and 104-120 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Inaba *et al., Intern. Rev. Immunol.* **6**: 197-206, 1990 ("Inaba"), in view of Aldovini *et al., Nature* **351**: 479-482, 1991 ("Aldovini").

Claim 84 also stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Inaba, in view of Aldovini *et al.,* and further in view of Caux *et al., Blood* 75: 2292-2298, 1990 ("Caux"), as evidenced by Romani *et al., J. Exp. Med.* **180**: 83-93, 1994 ("Romani").

Applicants respectfully traverse these grounds for rejection.

Applicants have addressed both of these 35 U.S.C. §103(a) grounds for rejection together because they are both based on Inaba as the primary reference.

Applicants respectfully aver that the antigen-activated dendritic cells are not the same as the so-called 'dendritic cells' described by Inaba. Not only is the process used to make Applicants' claimed cells different from the process described by Inaba, but the cells themselves that result from the different processes are also different.

The so-called 'dendritic cells' of Inaba cannot be pulsed with native protein antigen after a *single day* in culture (see page 198, first full paragraph, which states, "After a day in culture, however, the dendritic cells cannot be pulsed with native protein antigen."). Inaba later states that his 'dendritic cells' can "only capture antigens for a short period." (page 198, paragraph spanning pp. 198-99). Thus, the so-called 'dendritic cells' of Inaba can uptake native protein antigens for only a short time, and lose this ability after a mere day in culture.

In contrast, the Application describes the uptake of native protein antigen by dendritic cells *several days* after the cells are cultured. For example, in Fig. 13, the Application provides results showing that dendritic cells which were cultured for 6 days in GM-CSF, then exposed for 2 hours to BCG antigen, and then cultured another 2 days in GM-CSF were still able to express antigen from the native BCG antigen that they had been pulsed with. In other words, before the cells' initial exposure to BCG antigen, the cells had been cultured for *six days*, and were still able to uptake, process, and present BCG antigen.

Thus, the cells of Inaba are not the result of the same process as Applicants' claimed cells, nor are the cells of Inaba the same cells as Applicants' cells.

Moreover, because the cells of Inaba, are not able to be cultured for more than a single day, the ordinarily skilled artisan would realize that Inaba's so-called 'dendritic cells' cannot be enriched and expanded, as is required by the presently claimed composition. Culturing the cells of Inaba for longer than one day will cause them to lose their ability to uptake native protein antigen. Thus, the ordinarily skilled artisan would realize that if an attempt is made to enrich and expand the cells of Inaba, the cells of Inaba can no longer uptake antigen, and so cannot be antigen-activated, as is required by the present claim.

Accordingly, the cells of Inaba are simply not the same as those of the claimed invention.

The second cited reference, Aldovini, simply describes the BCG antigen. Aldovini makes no mention of dendritic cells, much less dendritic cells that, unlike the so-called dendritic cells of Inaba, are able to uptake antigen for processing and presentation after being cultured in GM-CSF. There is no suggestion or motivation provided by either Inaba or Aldovini to combine

the teachings of these two references. Absent such motivation, the combination of these two references cannot render the present invention obvious.

Moreover, even if, lacking motivation, the ordinarily skilled artisan were to combine the teachings of Inaba with Aldovini, he would still not have arrived at the presently claimed invention. Neither reference describes the enriched and expanded population of antigen-activated dendritic cells of the present claim. As each of the cited reference fails to teach or even suggest the claimed composition, their combination cannot arrive at that claimed composition. Accordingly, claims 89, 91-92, 94-95, 99, 101, and 103-120 are non-obvious in view of the teachings of Inaba and Aldovini. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Applicants also respectfully traverse the rejection of claim 84 was also rejected over Inaba in view of Aldovini and Caux, as evidenced by Romani *et al.* (1994).

Inaba and Aldovini have been discussed above.

Caux merely describes the effects of TNFs on the growth of human CD34+ cells. However, nowhere does Caux mention the word "dendritic cell". There is, in short, no reason for the ordinarily skilled artisan to combine the teachings of Caux with those of Inaba and Aldovini.

The Office Action has cited Romani as allegedly teaching that "culture of CD34+ stem cells in GM-CSF and TNFα will result in dendritic cell products." (see Office Action mailed July 2, 2002; p. 7). Presumably, the Office Action is arguing that the cells resulting from the method described by Caux, while not stating so, are inherently dendritic cells based on Romani (which was published after the earliest priority date of the Application).

Applicants respectfully aver the ordinarily skilled artisan could not have known, at the time of filing, that the cells described by Caux were dendritic cell products. As the Federal Circuit has pointed out, "That which may be inherent is not necessarily known. Obviousness cannot be predicted on what is unknown." In re Rijckaert and van der Kop, 9 F.3d 1531, 1534

(Fed. Cir. 1993). No guidance is provided in Caux to combine its teachings with those of Inaba and Aldovini. As such, their combination cannot render the claimed invention obvious.

Based on these remarks, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

II. Rejections Under 35 U.S.C. §112, First Paragraph

Claim 109 stands rejected under 35 U.S.C. § 112, first paragraph. The Examiner opines that the specification lacks written description to show the inventors were in possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse this ground of rejection.

The Office Action has asserted that the basis cited for this claim, in original claim 28 and at pages 29-30 of the specification, lack specific support for the claim language "cell aggregates are subcultured from about one to five times."

Applicants respectfully points out that the Federal Circuit has held that "claimed subject matter does not need to be described in *haec verba* in the specification for that specification to satisfy the description requirement." In re Wright, 866 F.2d 422, 425 (Fed. Cir. 1989). Applicants respectfully aver that the paragraph of the specification spanning pages 29-30 describes the subculturing of cell aggregates (see, e.g., page 29, lines 21-22 "cell aggregates may be serially subcultured multiple times"; page 29, lines 27 "aggregates are subcultured..."). Applicants aver that it is clear to the ordinarily skilled artisan, upon reading page 29, lines 34-35, that the "cells" described as being subcultured between about one to five times are cell aggregates, particularly given the language of original claim 28, which states that the cell aggregates are serially subcultured one to five times.

Accordingly, Applicants submit that claim 109 is fully supported by the specification. This ground for rejection should be reconsidered and withdrawn.

Claims 84, 89, 91-92, 94-95, 99, 101, and 103-120 are newly rejected under 35 U.S.C. §112, first paragraph, as lacking written description to show the ordinarily skilled artisan that the inventors were in possession of the claimed invention at the time the application was filed. Specifically, the Office Action has asserted that there is support in the specification for an enriched and expanded population of dendritic cell precursors, but no support for an enriched and expanded population of antigen-activated dendritic cells.

Applicants respectfully traverse this ground of rejection.

The Application is replete with descriptions of numerous methods for obtaining an enriched and expanded population of antigen-activated dendritic cells. For example, at page 68, line 20, through page 69, line 34, dendritic cell aggregates are describes as being exposed to latex particles, and to live BCG mycobacteria. As stated at page 69, line 24, the mature dendritic cells were isolated from the cultures exposed to BCG mycobacteria. After two days of further culture, the specification states that "Because many mature dendritic cells formed during the chase period, the number of Ia-rich progeny had increased four fold." (page 69, lines 32-34).

Thus, Applicants aver that "an enriched and expanded population of antigen-activated dendritic cells" is fully supported by the specification. Accordingly, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

Claims 84, 89, 91-92, 94-95, 99, 101, and 103-120 are newly rejected under 35 U.S.C. §112, first paragraph, as lacking written description to show the ordinarily skilled artisan that the inventors were in possession of the claimed invention at the time the application was filed. Specifically, the Office Action has asserted that there is no written description support evidencing that the Applicant was in possession of a "modified antigen" or a method for "antigen modification".

Applicants traverse this ground for rejection.

Applicants respectfully aver that support for the terms "modified antigen" and "antigen modification" can indeed be found in the Application as filed (see, *e.g.*, page 41, lines 29 through page 42, line 24)

Accordingly, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

Claim 84, 89, 91-92, 94-95, 99, 101, and 103-120 are also newly rejected under 35 U.S.C. §112, first paragraph, because "the specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation." (Office Action, page 5).

Applicants respectfully traverse this ground for rejection.

The Office Action has asserted that because Applicants have distinguished their claimed cells over those described by Inaba, the claimed cells are not enabled since Inaba states that cells cultured for even a day cannot be pulsed with native protein antigen. (Office Action, p. 5, citing p. 198 of Inaba). The Office Action has stated that, because two of the three named inventors of the Application are listed as authors of the Inaba paper, "the Inventors themselves teach that the process of the instant claims cannot function as claimed." (Office Action, p. 5).

Applicants disagree with this characterization of the Inaba reference.

Applicants respectfully point out that one of the inventive concepts provided by the Application is a method for enriching and expanding antigen-activated dendritic cells. Indeed, in Fig. 13, the specification describes the presentation of BCG antigen by dendritic cells, which were 6 day bone marrow cultures induced with GM-CSF. By raising this ground for rejection, the Office Action is disregarding the teachings of the specification itself, which demonstrates that the claimed composition can be achieved by the process of the claim.

The Inaba reference has been discussed at length above. Applicants respectfully aver that the reason the cells described by Inaba were not able to process and present antigen after a mere

one day in culture was because the cells were not cultured the presence GM-CSF (as is required in claim 101, from which all other claims depend). Indeed, it was the discovery that culturing dendritic cell precursors in the presence GM-CSF would result in dendritic cells capable of being activated by antigen that led to the invention described in the Application (see, *e.g.*, specification at page 25, lines 19-20). Thus, even if the starting cells of Inaba may have been the same as the starting cells that result in the claimed composition (and note that Applicant is not conceding that the starting cells are, in fact, the same), because the process is different, the resulting dendritic cells that are the subject of the claimed composition are different from those described by Inaba.

Thus, the Office Action's assertion that Inaba proves the claims are not enabled by the Application is without merit. Based on these remarks, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

III. Nonstatutory Double Patenting Rejection

Claims 84, 89, 91-92, 94-95, 99, 101, and 103-120 are provisionally rejected for obvious-type double patenting over claims 45 and 46 of copending Application No. 10/287,813.

Applicants respectfully request that this ground for rejection be held in abeyance until allowable subject matter is indicated.

Conclusion

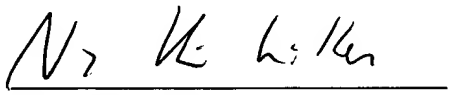
In view of the foregoing remarks, Applicants respectfully submit that this application is in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

A Petition for a one (1) month Extension of Time under 37 C.F.R. § 1.136(a) is filed concurrently herewith, which extends the response period from May 3, 2004 to June 3, 2004.

The Petition authorizes the PTO to charge the one month extension fee of $55 to our Deposit Account No. 08-0219, which reflects Applicants' Small Entity Status.

If there are any other fees due in connection with the filing of these papers, please charge the fees to our Deposit Account No. 08-0219. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,



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